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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/141,496	10/22/1993	MARCUS F. BOEHM	203268	7787
20985 7590 03/29/2007 FISH & RICHARDSON, PC P.O. BOX 1022 MINNEAPOLIS, MN 55440-1022			EXAMINER DESAI, RITA J	
			ART UNIT 1625	PAPER NUMBER
SHORTENED STATUTORY PERIOD OF RESPONSE			MAIL DATE	DELIVERY MODE
3 MONTHS			03/29/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No. 08/141,496	Applicant(s) BOEHM ET AL.	
	Examiner Rita J. Desai	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 December 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 71, 74, 75 and 79-81 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 71, 74, 75 and 79-81 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 71, 74, 75, 79-81 are pending.

The rejection of claims 71, 74, 75, 79-81 under 35 USC 103 has been withdrawn. Applicants have amended claim 71 to limit Y to be a N, O or an S. Hence the rejection on claim 71 and 79 has been withdrawn.

Applicants' claims 74, 75, 79 and 80 have a group R₅ which is Or₅ and the Maignan et al reference has a h which is an unobvious variant.

However the new matter rejection on the claims 71, 75, 79 and 81 still stands and will be discussed later.

The new matter rejection on claims 71, 75, 79 and 81 still stands.

Applicants argue that they have support for an alkyl group because example 51 on page 18 teaches a compound with the R''' R'''' being a methyl.

This may lend support for it to be a methyl when Y is ac and R₅ is a methyl, but it does not lend support for an alkyl group for the full scope of formula I and II.

The rejection still stands.

New Grounds of rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

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pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 71, 74, 75, 79-81 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

- 1) Y being a C, does not reasonably provide enablement for Y being a N, S or O and
- 2) enabling for a few compounds wherein y is a C and some assays, does not enable them for a "pharmaceutical use".

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

1) The breadth of the claims: The instant claims encompass many compounds from an aromatic carbocyclic moiety to an aromatic heterocyclic moiety having many large electron withdrawing and bulky groups substituted on it. These compounds cover a very wide range of compounds.

2) The nature of the invention: The invention is a substituted compound that has pharmaceutical use.

3) The state of the prior art: The state of the prior art is that the drugs and the enzymes react in a lock and key mechanism and the structure of the compound has to be specific. Even a difference of a methyl group versus a hydrogen changes the properties altogether. A good example is a theophylline versus caffeine. They differ by just a methyl group but one of them has a pharmaceutical use as a bronchodilator. There is no absolute predictability and no established correlation between the different substitutions on a core that they would all behave in the exact same way. The existence of these obstacles establishes that the contemporary

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knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

4) The level of one of ordinary skill: The ordinary artisan is highly skilled.

5) The level of predictability in the art: It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. The level of unpredictability in the art is very high. As can be seen by the compounds which differ by a methyl group and show different properties, for e.g. theophylline and caffeine. One of them is a bronchodilator and they differ only by a methyl group.

The state of the art shows that it is extremely unpredictable. Pharmaceutical use is more so and is also dose dependent. Higher doses may be highly toxic.

6) The amount of direction provided by the inventor: The inventor provides very little direction in the instant specification. There are no examples with the Y being a N, S or O. There are no starting materials for the same disclosed. A key issue that can arise when determining whether the specification is enabling is whether the starting materials or apparatus necessary to make the invention are available. In the biotechnical area, this is often true when the product or process requires a particular strain of microorganism and when the microorganism is available only after extensive screening. The Court in In re Ghiron, 442 F.2d 985, 991, 169 USPQ 723, 727 (CCPA 1971), made clear that if the practice of a method requires a particular apparatus, the application must provide a sufficient disclosure of the apparatus if the apparatus is not readily available. The same can be said if certain chemicals are required to make a compound or practice a chemical process. In re Howarth, 654 F.2d 103, 105, 210 USPQ 689, 691 (CCPA 1981).

There is no data in the specification that the compound indeed do have some "pharmaceutical" use. On pages 91-99 there is some IC50 values for cell proliferation. However there are no in vivo tests for the full scope of the claims that these compounds do indeed "treat" cell proliferation.

7) The existence of working examples: the lack of data, in view of the unpredictability especially treating to this day of cancer is unknown let alone at the time of applicants filing the application, does not enable the using of the compounds. There are also no doses given that would treat diseases. As applicants specification recites a laundry list of diseases related to the RAR receptors. See Applicants specification on page 83 clearly teaches that RAR is associated with

skin related processes (e.g., acne, psoriasis, aging, wrinkling, and the like); in vivo modulation of programmed cell death (apoptosis); in vivo modulation of malignant cell development, such as occurs, for example, in acute promyelocytic leukemia, mammary cancer, prostate cancer, lung

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cancer, cancers of the aerodigestive pathway, skin cancer, bladder cancer, and sarcomas; m vivo modulation of premalignant lesions, such as occurs with oral leukoplakia and the like; m vivo modulation of auto-immune diseases such as rheumatoid arthritis; m vivo modulation of fatty acid metabolism; and the like.

8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: Since there are no working examples, and the art is highly unpredictable, the amount of experimentation is very high and burdensome.

Taking the above eight factors into consideration, it is not seen where the instant specification enables the ordinary artisan to make and/or use the instantly claimed invention.

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

Substantiation of use and scope is required when the use is "speculative", "sufficiently unusual", or not provided in the specification, *Ex parte Jovanovics*, 211 USPQ 907, *In re Langer*, 183 USPQ 288, *Hoffman v. Klaus*, 9 USPQ2d 1657, and *Ex parte Powers*, 220 USPQ 924 concerning the type of testing needed to support *in vivo* use claims. Also see the MPEP § 2164.03 for enablement requirements in the structure sensitive arts of pharmacology and medicinal chemistry.

Genetech Inc Vs Nova Nordisk 42 USPQ 2d 1001.

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"A patent is not a hunting license. It is not a reward for search but compensation for its successful conclusion and patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Conclusion

Claims 71, 74, 75, 79-81 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday, flex time..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thomas McKenzie can be reached on 571-272-0670. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Rita J. Desai
Primary Examiner
Art Unit 1625

RJ Desai
3/27/07

R.D.
March 27, 2007